

# DIURETIN-KNOLL AS A DIURETIC:

REPORTS ON CLINICAL EXPERIMENTS.

KNOLL & Co., MANUFACTURING CHEMISTS  
LUDWIGSHAFEN o/RHINE (GERMANY).

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Since “Diuretin-Knoll” was first recommended by Prof. v. Schroeder, Heidelberg, and Prof. Gram, Copenhagen, as a powerful diuretic for therapeutical application, extensive trials have been instituted with it in a series of large clinics, such as those of:

PROF. DRASCHE-Vienna (assistant physician: DR. PFEFFER)	[p. 2]
PROF. H. BABCOCK-Chicago . . . . .	[p. 11]
PROF. FRAENKEL-Berlin (assist. phys.: DR. SCHMIEDEN)	[p. 13]
DR. G. MERKEL-Nürnberg (assistant physician: DR. KRESS)	[p. 15]
PROF. ERB-Heidelberg (assist. phys.: DR. A. HOFFMANN)	[p. 17]
PROF. v. SCHROETTER-Vienna (assistant physician: DR. M. KORITSCHONER)	[p. 18]
PROF. SENATOR-Berlin (assist. phys.: DR. G. SIEFART).	[p. 18]
DR. SCHRAUB-Magdeburg	
PROF. TSCHUDNOWSKY-St. Petersburg (assistant physician: DR. TH. GEISLER)	[p. 19]
PROF. DUJARDIN-BEAUMETZ-Paris (assistant physician: DR. KOUINDJY-POMERANTZ)	[p. 19]
PROF. GRAM-Copenhagen.	

In all these trials the remedy has justified its reputation in the most brilliant manner, as is evidenced by the following abstracts from treatises which have appeared on the subject. All authors agree in pronouncing “Diuretin-Knoll” a diuretic of preëminent activity and of high importance.

Diuretin has yielded striking results in cases where Digitalis, Strophantus, etc., proved of little or no value.

Over Calomel it has the advantage of being perfectly free from any toxic action.

We invite attention to the following reports.

LUDWIGSHAFEN °/RHINE, December 1891.

KNOLL & Co.  
MANUFACTURING CHEMISTS.

From the medical wards of Prof. Drasche in the Vienna  
Imperial General Hospital.

## Experiments with Diuretin-Knoll

by

Dr. Siegmund Pfeffer.

*(Centrallblatt für die gesammte Therapie 1891. No. 8).*

**Prescription.** We employed Diuretin in about 40 cases; the daily dose amounted to  $1\frac{1}{4}$  drms. and was increased in many cases to  $2\frac{1}{2}$  drms. in 24 hours.

**Kinds of Disease.** The remedy was ordered, principally, in cardiac dropsy (vitium cordis, arterio-sclerosis, cor. adiposum), acute Bright's disease, chronic nephritis, pleuritis, tuberculosis membr. seros. and cirrhosis hepatis.

**Cardiac dropsy.** If we consider first the cases of cardiac dropsy, the remedy proved here to be a valuable diuretic, in that, within a short time, the quantity of urine increased to 5 or 6 litres daily. The action showed itself soon after the remedy had been taken, in many cases after only 36 to 48 hours, in a few instances, not until it had been used some time, even though from the commencement, a merely slight increase in the quantity of urine was to be observed. I remark, at the same time, that in a few isolated cases of this class, where, at first, Diuretin was without effect, an abundant flow of urine was produced, after repeated doses, other diuretics having been given in the meantime with slight benefit.

The excretion of urine adjusted itself, especially in cardiac dropsy, according to the extent and volume of the exudation, though it must be pointed out, that the reduction of the dropsy did not always keep pace with the quantity of urine. We had under observation, a case of vitium cordis with oedema, in which only a slight diminution of the dropsy was effected, even when 2 to 3000 ccm of urine were passed daily for a prolonged time. The subjective feeling was however improved and the urgent symptoms disappeared.

The cases of peritoneal tuberculosis with oedema and ascites particularly, showed that in spite of large quantities of urine and numerous diarrhœic motions, in one case, scarcely any

reduction could be detected in the oedema and, in the second, only a stationary condition. The majority of cases of cardiac dropsy, however, soon ran a favourable course, dropsy disappearing, and subjective feelings rapidly improving. The patients recovered with surprising rapidity and could again resume their avocations.

As to the duration of the effect of the remedy after its use has been suspended, the investigations do not quite agree. We did see, though seldom, an increased quantity of urine under such circumstances even 2—3 days as proved by actual measurement and chemical testing; in most cases we could not determine the after-effect to last longer than 24 hours at the outside.

Somnolence, a feeling of giddiness, head-ache and profuse diarrhœa, were observed as bye-effects of the action of Diuretin; the same symptoms were recorded by Gram but other authors reported that none were seen with the exception of the diarrhœa. This last has little connection with the Diuretin treatment; we often saw it in chronic nephritis, as also, in cases of cardiac dropsy at a time, when the Diuretin cure was not commenced. On the other hand, it must be acknowledged that in many cases, the diarrhœa disappeared with the suspension of the Diuretin; in most cases however it ceased of itself after a time and did not again appear. We ordered Diuretin, in powder form, up to 45 grains for healthy persons, who suffered from passing constipation, without producing any stools. It seemed, therefore, possible, that the remedy produced quite a different effect upon the sound and the diseased organism and that this is the case is proved by the fact, that, in healthy persons to whom Diuretin was given experimentally, we did not see — agreeing in that respect with Hoffmann — any increase in the quantity of urine.

Somnolence and headache we saw only at the beginning and they were of but short duration; in cardiac dropsy exceedingly rare.

The urine, the specific gravity of which as the tables show, corresponded to the volume, had few characteristics. The albumen-content was various; in cases of cardiac dropsy where the quantity of albumen mostly did not reach any high level, there was no noteworthy alteration; the quantitative albumen-estimation, according to Esbach, exhibited no difference worth mentioning.

In referring to the cases of nephritis, we must distinguish between the acute and chronic forms. In the first, Diuretin proved to be without effect, but in the chronic variety, particularly in the secondary shrivelling of the kidneys favourable, nay sometimes astonishing, results, were obtained.

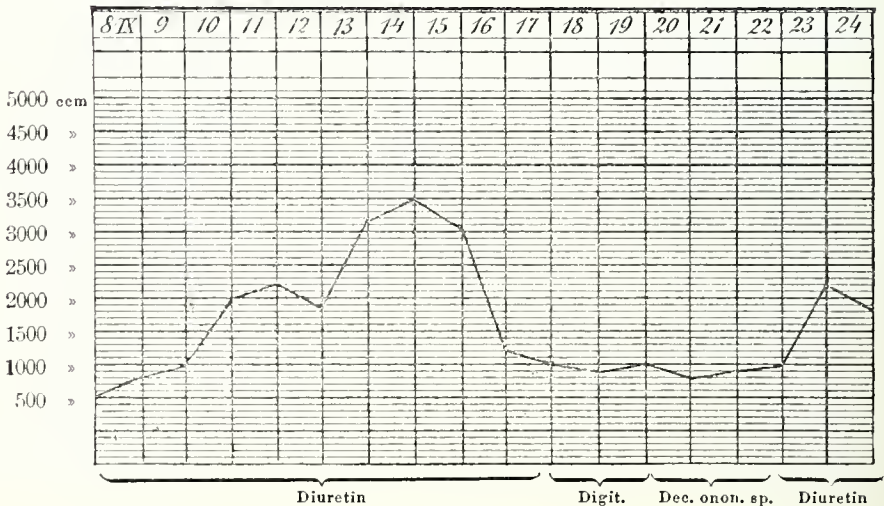


As an example of the action of Diuretin in chronic nephritis, the following clinical histories may be cited; they show how prompt and effective the action of the remedy is and may simultaneously illustrate the inferior virtue of the other diuretics.

G. T., furrier, 28 years, dates his illness from eight weeks back, and ascribes it to a cold; his face and extremities began to get swollen. This condition lasted three weeks and the oedema disappeared. Symptoms recurred four weeks before he came under observation.

Present condition: Delicate frame fairly well nourished. Face oedematous, radial artery very tense, second aortal sound accentuated. Left ventricle hypertrophied. Quantity of urine **600, 700, 500** ccm. In the sediment granulated and hyaline casts.

Date	Therapy	Urine ccm.	P.	R.	Blood pressure	Remarks
8./9.	Diuret. 1 1/2 drms.	800	84	28	100	Some fluid motions
9.	»	1000	80	24	100	Headache, once sickness
10.	»	<b>2000</b>	90	20	115	Subjective well-being
11.	»	<b>2500</b>	80	24	120	Oedema in face less
12.	»	1800	80	24	115	—
13.	»	<b>3300</b>	80	24	130	—
14./9	»	<b>3500</b>	90	24	130	Oedema decreasing
15.	»	3000	90	24	130	—
16.	»	1200	90	24	130	A firm stool daily
17.	Inf. digit.	1000	72	18	125	—
18.	»	950	72	18	120	—
19.	Dec. ononid. spin. c. liq. kali acet	1000	72	18	120	—
20.	»	800	72	18	120	Patient feels unwell
21.	»	900	72	18	110	Oedema increasing
22.	Diuretin	1000	80	24	110	—
23.	»	<b>2500</b>	80	24	115	—
24.	»	1800	80	25	125	Oedema gone.
25.	Discharged	better				



Of two cases of Cirrhosis hepatis, I give one clinical history, in which, also, the favourable action of Diuretin is visible. Cirrhosis hepatis.

F. P., 43 years, tailors assistant; was twice under hospital treatment in 1889. The patient complained then of jaundice, swelling of the abdomen, oedema of the lower extremities and later dyspnœa. Access of the same symptoms induced the patient to again seek aid at the hospital.

Delicate frame, somewhat wasted. Jaundice. Nothing abnormal in the lungs. Cardiac tones pure. Abdomen tense, liver extending three finger-breadths below the ribs. Ascites. Oedema of the lower extremities. Skin dry, scurfy. Confessed to drinking habits.

Diagnosis: Cirrhosis hepatica.

Therapy: Inf. digitalis.

Volume of urine: **900 ccm.**

Date	Therapy	Urine ccm.	Blood pressure	R e m a r k s
21./7.	Diuretin 1½ drn.	1200	100	P. 100. R. 20. T. 37.1°
22.	»	<b>1800</b>	100	P. 104. R. 28.
23.	»	1300	110	P. 108. R. 24. T. 36.1°
24.	»	1000	115	P. 116. R. 24. T. 36.8°
25.	»	1100	120	P. 96. R. 24. T. 38.0°
26.	»	1300	110	P. 100. R. 16
27.	»	1400	120	P. 96. R. 20
28.	»	1400	120	P. 104. R. 20
29.	»	<b>2700</b>	120	P. 108. R. 20
30.	»	<b>2600</b>	120	P. 112. R. 24
31.	»	1800	120	P. 116. R. 24.
1./8.	»	1700	115	Oedema disappeared
2.	»	<b>4000</b>	135	P. 116. R. 24
3.	»	<b>4200</b>	135	P. 96. R. 20
4.	»	3500	120	P. 96. R. 20
5.	»	2700	120	P. 96. R. 20
6.	»	1500	120	P. 96. R. 20

The beneficial action of Diuretin, in cases of pleuritis, Pleuritis. which was observed by many authors, was not manifested in our cases, for the volume of urine increased only to a small degree and the exudation was not more quickly absorbed than when other therapeutical measures were taken.

The action of the remedy in a case of anaemia with oedema is evidenced by the following history.

E. G., 27 years, soap boiler's wife, up to three years ago always healthy. From some unknown cause, weakness developed and oedema of the lower extremities. These symptoms lasted some time and disappeared; on account of constant weakness and loss of appetite the patient sought the hospital.

Patient presented the appearance of an advanced anæmic with glandular enlargement in the maxillary, sternoclavicular and axillary regions. "Bruit de diable" over the veins of the neck.

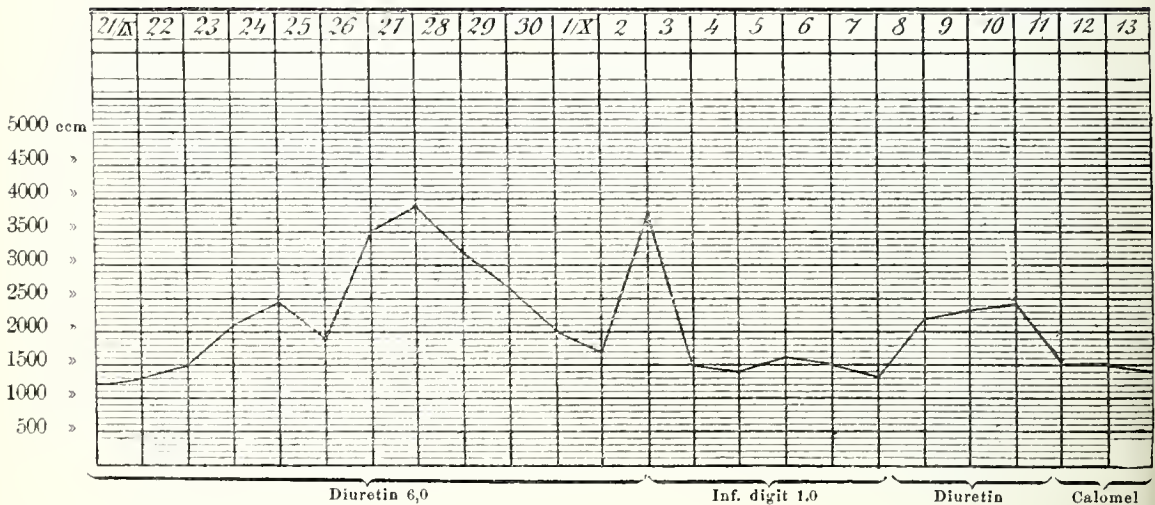
Over the left ventricle a blowing sound, becoming sighing towards the end; near the pulmonalis this had a scraping rustling character.

Poikilo-, macro- and micro-cythoses were found in the blood.

Diagnosis: Anæmia.

Volume of urine: **700 ccm.**, of sp. gr. 1020 and containing some albumen.

Date	Therapy	Urine ccm	Blood pressure Rad.	Re m a r k s
21./9.	Diuretin 1½ drm.	700	110	3 liquid stools
22.	»	1000	110	3 liquid stools
23.	»	1600	115	Headache, weakness.
24.	»	<b>1950</b>	115	Diarrhœa
25.	»	1400	120	—
26.	»	<b>3000</b>	115	Oedema less
27.	»	<b>3900</b>	130	—
28.	»	<b>2700</b>	120	Subj. well-being
29.	»	2200	120	—
30.	»	1500	120	1 liquid stool
1./10.	»	1200	115	1 semiliquid stool
2.	»	<b>3300</b>	115	2 solid stools
3.	Diuret. suspended	1000	115	Oedema gone
4.	»	950	100	2 liquid stools
5.	»	1100	95	—
6.	Inf. digitalis	1000	100	3 liquid stools
7.	»	800	110	Oedema reappeared
8.	Diuretin	1700	120	—
9.	»	1800	130	—
10.	»	1900	195	Urine passed with the stool
11.	Calomel	1000	80	—
12.	»	1000	90	—
13.	»	900	110	Oedema decreased.





The history of the cases and the tables show that during the Diuretin treatment of cardiac dropsy there was an increase of blood pressure. The measurements were taken daily with the v. Basch sphygmo-manometer and the rise of blood pressure had, in many cases, a certain relationship to the quantity of urine excreted, in that the greatest pressure coincided with the largest volume of urine.

Action on blood pressure.

The question now arises: Is this increase of blood-pressure identical with that of caffeine, i. e., could it be explained as an action upon the vasomotor centre?

Against this possibility there are two things. Firstly, the volume of urine excreted was incomparably larger than has been hitherto produced by caffeine or any other diuretic. Of far greater weight however was the behaviour of the pulse and heart, which gives Diuretin a new property, so far appreciated only by Hoffmann. We know that, in valvular insufficiency, if the dropsy which makes the circulation so difficult, disappear, all resistance will also be removed, the urgent symptoms abate, a quiet cardiac action sets in and the patient recovers. And yet we see all these effects after a short period of the Diuretin treatment and before the dropsy has altered to any extent.

The pulse was more powerful, the dyspnœa abated and the irregularity of the heart's action disappeared. We reproduce pulse-curves taken from a few patients before and during the Diuretin treatment and in which, as the figures themselves show, a characteristic alteration is perceptible.

M. R., 35 years, business manager.

Treated for acute rheumatism of the joints in 1883 in the V. med. department. The first attack 10 years ago. Condition of the heart in 1883:

Over the aorta a dull systolic tone and a short diastolic tone with a supplementary short gentle murmur.

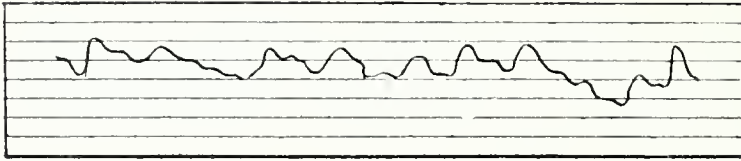
Since then frequent attacks of dyspnœa and palpitation, sleeplessness and partial oedema. On September 20<sup>th</sup> entered the hospital again in consequence of increasing troubles.

Advanced dyspnœa. Cyanosis of face. Pulse rapid. Heart dullness enlarged in all dimensions. Apical beat two finger-breadths outwards from the mammillary line in the sixth intercostal space. Two murmurs audible at the apex, one loud systolic terminating with a sound, the other soft, sighing, diastolic and long drawn out. Over the aorta a very loud sighing diastolic murmur which is also audible over the carotid. Oedema. Urine sparse. Albumen and crystals of uric acid and double phosphate of ammonia and magnesia. Pulse capillary.

Diagnosis: Aortic valvular insufficiency.

Volume of urine: 400 ccm. Sp. gr. 1025.

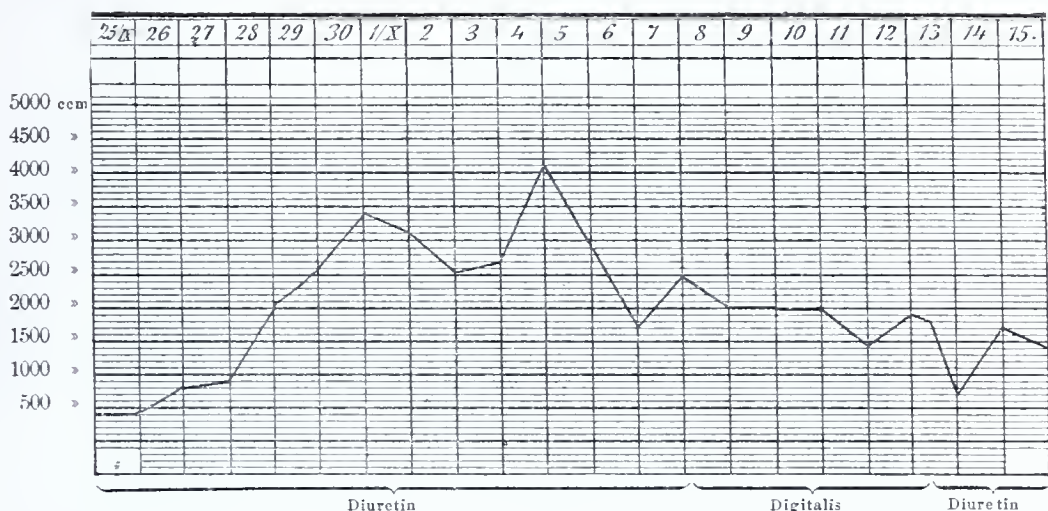
Pulse curve on admission.



Pulse curve on the sixth day of the treatment.



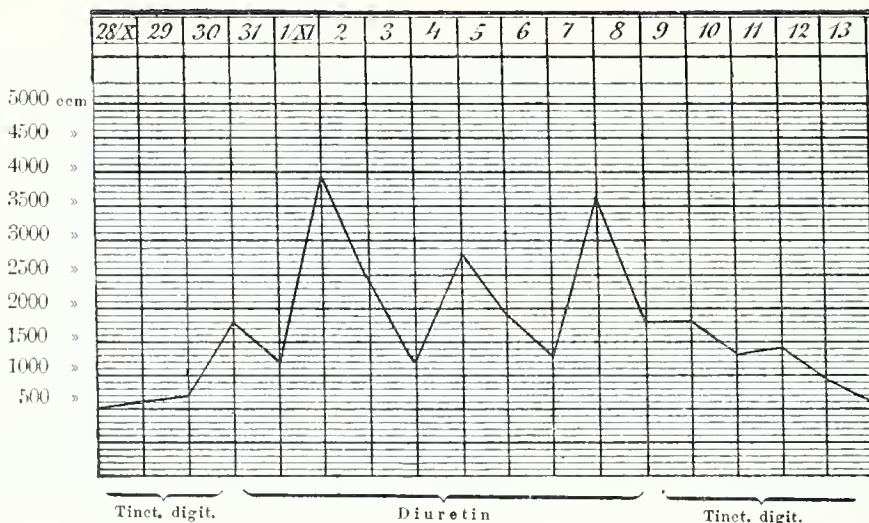
Date	Therapy	Urine ccm.	Blood pressure	Remarks
25./9.	Diuretin 1½ drm.	400	150	2 liquid stools. P. 96
26.	»	800	150	P. 96. R. 20
27.	»	900	145	Headache. P. 72. R. 20
28.	»	2000	155	{ Well-being. Patient slept well. Oedema less
29.	»	<b>2600</b>	160	P. 80. R. 20. Stools normal
30.	»	<b>3400</b>	165	P. 80. R. 24
1./10.	»	<b>3200</b>	165	Well-being
2.	»	2500	170	No dyspnœa
3.	»	2700	165	Oedema disappeared
4.	»	<b>4100</b>	170	Dyspnœa in the night
5.	»	2900	170	{ Pains in the joints P. 105 R. 28
6.	»	1700	170	Subj. well-being
7.	»	2500	175	No rheumatic pains
8.	»	2000	175	P. 80. R. 24.
9.	»	2000	175	One firm stool daily
10.	»	1400	175	P. 96. R. 40. Oedema gone
11.	»	1900	180	P. 80. R. 24
12.	Inf. digitalis	1800	170	Dyspnœa
13.	Diuretin in the evening	700	165	Well-being
14.	»	1700	180	»
15.	»	1400	170	»



On October 26<sup>th</sup> 1890 the patient was again brought into the hospital on account of violent attacks of dyspnœa and palpitation. Patient enormously dyspnœic: face strongly cyanotic. Hearts action very irregular, diffuse pulsation perceptible in the region of the heart. Free liquid in the abdomen: liver enlarged. Oedema.

Urine containing albumen. Sp. gr. 1017. Volume 100 ccm.

Date	Therapy	Urine ccm	Blood pressure	Remarks
29./10.	Tinct. digitalis Aether. } inject.	100, 500, 600	120	Attacks of dyspnœa
	Diuretin 6,0 (1½ drgm): } 200,0	700	125	Stenocardiac attacks
30.	»	1800	130	Attacks less. Sleeplessness
31.	»	1250	130	—
1./11.	»	3900	140	Subjectively feels better
2.	»	2450	145	No dyspnœa
3.	»	1200	145	Hearts action regular
4.	»	2800	145	Oedema less
5.	»	1900	155	One firm stool daily
6.	»	1350	160	—
7.	»	3600	160	General well-being
8.	»	1800	160	Oedema disappeared
9.	»	1800	150	—
10.	»	1300	150	—
11.	Tinct. digitalis	1400	150	—
12.	»	900	140	Dyspnœa. Palpitation.
13.	»	600	150	—
14.	Discharged, uncured, at his own desire.			



From this behaviour, we must differ from Gram and ascribe to Diuretin, beside the action on the renal epithelium, also an effect upon the cardiac apparatus. In this we are in accord with the results of Hoffmann's investigations.

That the renal action is the greater, cannot be contested, but the sole effect, in the sense of Gram and Schröder, it is not.

As to the other diuretics, digitalis ought chiefly to be mentioned.

Though, in many cases, digitalis was far inferior to Diuretin in activity, yet we cannot consider the latter as a substitute for the former. If digitalis is of preponderant value as a cardiac, Diuretin proves itself to be preëminent as a diuretic, with a certain action on the heart which is quite subordinate to that of digitalis. The same may be said *mutatis mutandis* of the other diuretics.

If, in conclusion, we glance once again at the results obtained with diuretin in our clinic, we may sum up by saying, they demonstrate that Diuretin is a diuretic of remarkable value in cardiac dropsy and in chronic nephritis, of less virtue in cirrhosis hepatis and of no effect in Bright's disease and pleuritis.

Diuretin produces exceedingly few bye-symptoms and the action does not last long after its suspension.

The cases, in which, after fruitlessly trying most diuretics, we must resort to calomel, become gradually fewer and we shall always first ascertain the effect of Diuretin, before taking up the last weapon — the double edged diuretic, calomel.

## The remarkable effects of Diuretin in removing Dropsy

by

Robert H. Babcock. A. M., M. D.,

Professor of Clinical Medicine, Chicago.

*(New York Medical Journal 1891, July).*

The author, having briefly outlined the history of Diuretin, reports on a few cases of dropsy treated with it by him.

**Case I.** Mr B, aged 62 suffered for a long time from irregular action of the heart, arterio-sclerosis and digestive disturbances. At the beginning of March the pulse was weak, and arrhythmic; there was oedema of the lower extremities with anorexia and obstinate constipation.

All measures taken to regulate the pulse and stimulate the kidneys were of no effect. Digitalis and caffeine, exerted absolutely no effect upon the dropsy. Oedema steadily advanced, until, at the end of a week, it had involved the genitals and peritoneal cavity. The heart's action was bad and attacks of cardiac asthma were frequent and violent, while a hard cough, with scanty serous expectoration, increased the suffering.

Diuretin-Knoll was ordered; in the first 24 hours 90 grains, and 120 grains a day for four days. The result was astonishing.

The daily quantity of urine, previously  $1\frac{1}{2}$  pint, increased to 12 pints (after 90 grns. of Diuretin) and, subsequently, to 14 pints (after 120 grains). The oedema disappeared and the cough ceased to be troublesome. A week later the patient again resorted to Diuretin owing to a recurrence of slight ascites; at present he is far better than for months prior to his illness.

The author observed in this, as also in the next case, a marked improvement of the pulse, which became powerful and regular. Of the two possibilities, that the action of the remedy on the heart was direct, or indirect, the author inclined to the former, which was evidenced by a strengthening and regulation of the pulse.

**Case II.** Miss S, 18 years, has been confined to bed for nine weeks with heart disease. Examination revealed mitral stenosis with quick irregular pulse. Oedema of the feet and legs nearly to the knees. Liver enormously enlarged. Not much more than a pint of urine daily.

90 grains of Diuretin were given daily and continued for six days.

The urine, which unfortunately could not be all collected, increased to 6 pints. On the sixth day the oedema had practically disappeared. During the treatment the pulse became manifestly slower, stronger and perfectly regular.



After a time, oedema of the legs and ascites reappeared, with a very weak arrhythmic pulse, scarcely perceptible at the wrist. Diuretin was again given, with amazing success, for, after only two days, the oedema was greatly reduced, the pulse full and regular, pains had disappeared and a feeling of comparative well-being was experienced.

**Case III.** Patient was admitted into hospital, with the evidences of a chronic parenchymatous nephritis and general dropsy, at the end of March. The urine was scanty, about 2 pints in 24 hours, of high specific gravity and containing hyaline casts.

All the usual diuretics were useless: at length elaterin was given in frequently repeated doses of  $\frac{1}{10}$  grn, when, with free purging, the volume of urine increased to 73 ounces and the oedema began to disappear.

In order to study the action of Diuretin in this class of diseases, 90 grains were given daily. The volume of urine rose at once to 146 ounces and after 2 days, the patient begged to have the medicine discontinued. Oedema had entirely vanished, and, two days after the discontinuance of the medicine, the quantity of urine amounted to 161 ounces.

The author further communicates a case where a man of 61 years suffered from acute pleurisy with moderate effusion of the left base. Examination revealed moderate hypertrophy of the left ventricle, arterio-sclerosis and renal cirrhosis. The oedema which appeared while the patient was in the hospital could not be reduced by digitalis. Diuretin in 90 grn doses was also without effect, whilst 120 grns *pro die*, produced a doubling of the volume of urine voided and brought about the disappearance of the oedema.

The author sums up his conclusions as follow:

1. Diuretin-Knoll is a diuretic of great power and promptitude.
2. It is likely to succeed where digitalis, caffeine and their congeners fail.
3. In cases of cardiac dropsy with great feebleness of pulse and arrhythmia, it will strengthen and regulate the heart's action.
4. It must be given in doses of 90—120 grns daily.
5. It is best administered ~~either~~ in aqueous solution ~~or in~~ ~~gelatine-coated pills~~, since, if exposed to the air in powders, it undergoes change and insoluble theobromine is partially thrown out.

From the Town Hospital at Urban, Berlin.

*In-patient department of Prof. A. Fraenkel.*

## The Action of Diuretin

by

Dr. W. Schmieden,

Assistant physician.

*(Centralblatt für klinisch. Medicin 1891, No. 30).*

After the author has shortly reviewed the history of Diuretin-Knoll, he reports that since the summer of 1890, 31 patients have been treated for a longer or shorter time, with the remedy, in the in-patient wards of the Hospital above-named.

The Diuretin was mostly given in aqueous solution without correctives, in single doses of 15 grns ( $1-1\frac{1}{2}$  drm *pro die*) to adults and 8 grns (32—48 grains *pro die*) to children. In this form it was borne well and without exciting repugnance even after long periods. The simultaneous administration of sodium bicarbonate, recommended by Koritschner, proved to be unnecessary.

Of the 31 cases referred to, there were 15 of inflammation of the kidneys (13 chronic and 2 acute cases); 2 patients suffered from interstitial hepatitis complicated with nephritis and heart disease and the remainder from various affections of the circulatory system.

All the patients suffered with dropsy of various degrees, consisting either of oedema, ascites, and hydrothorax, or, of a combination of these forms. The diuretic effects were manifested as follows:

In a half of the cases of chronic nephritis, the increase in the volume of urine amounted to a third of the previous quantity up to nearly five times as much. In one case of nephritis after scarlet fever, Diuretin was brilliantly successful.

Among diseases of the heart, those complicated with chronic nephritis were treated with fair success if there were not too great disturbances of compensation, whilst the cases of pure valvular inefficiency, were most amenable to the

diuretic effect; in these cases an extraordinarily large and persistent flow of urine set in, which very soon freed the organism from the accumulated liquid. Results no less favourable must be recorded in the cases of arterial sclerosis and aneurysma arcus aortæ.

As a bye-effect of Diuretin, the author cites an increase in the pulse-rate not infrequently observed. So soon as this symptom appears, the use of Diuretin should, for a time, be suspended.

The author sums up his results in the following sentences:

1. Diuretin is an admirable diuretic in the majority of cardiac diseases, as well as in valvular affections and diseases of the vascular system (arterio-sclerosis).
  2. Diuretin has a favourable effect in a number of renal affections, both acute and chronic.
  3. The effect upon diuresis, which appears to consist in a direct influence on the secreting parenchyma of the kidneys, cannot in every case be predicted with certainty.
  4. No regulatory influence upon the activity of the heart and on the blood pressure is unmistakeably manifested.
  5. On the other hand, in a not inconsiderable number of cases, partly, after a preceding increase of the diuresis, and partly, without such, an increase in the pulse-rate with augmented arrhythmia is observed, which may lead to the suspension of the remedy.
  6. A prolonged after-effect on the diuresis, even in the cases with positive results, is, as a rule, as little evident with Diuretin as with calomel.
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From the Nuremberg Hospital.

(*In-patient wards of Dr. G. Merkel.*)

## The Action of Diuretin

by

Dr. Kress,

Assistant Physician.

(*Münchener Med. Wochenschrift 1891, No. 38.*)

The author reports on the results of the employment of Diuretin in a number of diseases which are classified in a table. There were 7 cases of renal inflammation, 3 acute and 4 chronic, which all developed more or less general dropsy; 8 affections of the heart, 3 cases of myocarditis and 5 of valvular insufficiency.

The author continues:

“If now, on the basis of the preceding table and a closer consideration of certain wellmarked cases, we study the action of Diuretin we are struck by its powerful diuretic effect. With the exception of the 2 cases of pleuritic exudation and the tubercul. pulmon. in the dropsical stage an increase of the volume of urine often four- or six-fold took place. This was so in 4 out of 5 cases of chronic nephritis, in 2 of acute renal inflammation, twice in 4 cases of cardiac valvular inefficiency, in 2 out of 4 cases of affections of the cardiac muscular tissue, in a cardiac valvular inefficiency with hepatic cirrhosis and in an acute hepatic enlargement. The day on which, after the dose of Diuretin, this increase of urine shows itself is very uncertain; sometimes it would be in the first and sometimes not until the sixth. After the discontinuance of the remedy the action lasts from 1—7 days. That frequently there is also an increase in the solid constituents of the urine, i. e. of the urea and urates, is shown by the second column “specific gravity”. In the majority of cases there appeared, with the increase in the quantity of urine a not inconsiderable augmentation of the specific gravity and in many cases the maximum of specific gravity coincided with that of the volume of the urine. What part the individual solid constituents play in the augmentation was not investigated. In no case had Diuretin a positively demonstrable influence

upon the albumen-content of the urine. It is true that in an acute renal inflammation the proportion of albumen rose suddenly with the urine maximum from 1,5 to 5 per mille but this must be regarded as an accidental occurrence since in no other case out of twenty was any noteworthy increase in the amount of albumen detected during the Diuretin treatment."

As to the contested question, whether Diuretin besides its stimulant action on the renal epithelium also exerts a direct influence on the heart, the author is of opinion that the improvement and regulation of the pulse during the administration of Diuretin is only to be traced to the removal from the circulatory system of the large quantity of liquid.

With reference to the secondary effects he says:

"We observed vomiting in one case so that we suspended the use of the Diuretin. When the administration was resumed after a fortnights pause the patient tolerated quite well 1½ drachms *pro die* in solution. In another case where the remedy was discontinued on account of nausea, its use was not returned to. The occasional appearance of slight diarrhœa did not prevent the continuance of the treatment, since in one case, though the use of the remedy was not suspended, the diarrhœa ceased after 3 days and in another, though it continued till the close to a slight degree, did not produce any disturbance of the general well-being. No alarming arrhythmia or acceleration of the pulse was seen: at any rate we observed, that this acceleration of the pulse which, as can be seen from the table, appeared in a few cases, mostly receded again to the normal during the Diuretin treatment without forming any indication for the discontinuance of the remedy."

"In conclusion, the question of course arises of itself, what place Diuretin will take in comparison with the diuretics hitherto known. In 6 cases Diuretin had an excellent diuretic action after digitalis, strophanthus, potass. bitart. borax. etc., had been previously given without success. Only in one case was Diuretin of no avail while digitalis was of good effect. It is superior to the other remedies of the same class, in the fact that it may be given continuously (in one case 3 ounces in 15 days) without any threatening symptoms whatever. As when repeatedly given in relapsing dropsy it does not diminish in activity but indeed frequently appears to become more powerful, is equally in favourable contrast to the properties of the diuretics we have hitherto possessed and especially of digitalis, the diuretic virtue of which when repeatedly administered to one and the same patient, often disappears."

"The results of our examination and observations may be summed up in the following sentences:



1) Diuretin is a powerful and true diuretic in that it brings about simultaneously an increased excretion of the aqueous and solid constituents of the urine.

2) Its action is due to a direct but non-irritating influence on the renal epithelium; it neither produces the appearance of albumen nor alters the proportion if already existent in the urine. The favourable effect upon the circulatory organs frequently seen is most probably of secondary origin.

3) Diuretin produces its diuretic action best in acute and chronic affections of the heart and kidneys, and in the first place are the acute renal inflammations and pure cardiac valvular inefficiency. Chronic nephritis and affections of the cardiac muscular system are also benefitted but in purely serous exudations, such as in the dropsical stage of tuberculosis, no success is to be expected from the treatment.

4) Diuretin can be administered continuously and in large doses (up to 2 drms *pro die*) without any dangerous effects and the diuretic action is not in the least enfeebled when the remedy is repeatedly given to one and the same patient."

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To these recent communications, the following extracts from the works of previous authors of eminence may be added.

Summing up a laborious treatise on the use of Diuretin,

**Dr. A. Hoffmann** (Clinic of Prof. Erb, Heidelberg) says (*Archiv f. experim. Pathol. and Pharm.* Vol. 28 p. 1):

"Diuretin is by virtue of the Theobromine it contains, a diuretic of excellent effect, which merits extended application in the treatment of general dropsy. In liquid exudations following on inflammation of the serous layers of the skin, it is of less and, in obstruction of the portal circulation, of no value.

The diuretic action is dependent upon a direct influence of the renal epithelium; at the same time, a certain favourable effect upon the circulatory organs, cannot be overlooked.

Given in the correct dose of  $1\frac{1}{4}$  drm *pro die* and in the right form, it is without any disturbing bye-effects. General well-being was beneficially influenced.

Diuretin exerts a diuretic effect under circumstances where other remedies of the same class, such as digitalis, strophanthus, caffeine, etc., have failed. It has no cumulative action and the effect quickly ceases so soon as the remedy is dis-

continued. Habituation and consequent diminished sensitive-ness to the action of the substance do not readily occur.

Diuretin can readily and successfully be ordered with other heart-tonics."

**Dr. M. Koritschoner** (Clinic of Prof. v. Schrötter, Vienna) says (*Wiener klin. Wochenschr.* 1890 Nr. 39):

"As regards the degree of action in the various diseases, the best results, on the whole, were obtained in cardiac dropsy. Then came disturbances of the portal circulation, while the most refractory were cases of nephritis. This order must be considered, however, only with regard to the absolute action of Diuretin. In comparison with other diuretics, the results were by far the most satisfactory, in chronic Bright's disease, for in these cases, in spite of the conspicuous failure of other remedies of the same class, the result of the Diuretin treatment was usually satisfactory."

Later on in the same treatise Dr. Koritschoner says:

"Referring to the remark of v. Ziemssen, in his address on the treatment of chronic Morbus Brightii, at the 9<sup>th</sup> Congress of Internal Medicine at Vienna, that we had not, at that time, any medicament, having a certain diuretic action in all cases, we must concede our preparation, (Diuretin-Knoll), a prominent place among remedies used as diuretics. With the exception of a few cases, in which all other remedies were equally inefficacious, it brought about a good result in many instances and, in a few, was extraordinarily successful. In view of the facts that the remedy proved harmless, even when given for prolonged periods, had no action on the heart, but apparently solely stimulated the renal epithelium, — in brief, since no contraindication for its use could be established — it can be confidently recommended for trial in all cases of dropsy. By reason of its useful and harmless properties even when given over a very long time it will have a special value for the treatment of chronic parenchymatous nephritis, in which, by most authorities, it is laid down as a therapeutical principle, that the kidneys should be subjected to a constant, non-irritating irrigation."

**Dr. G. Siefert** (Clinic of Professor Senator, Berlin) expresses himself in the following manner:

"These experiments confirmed the results obtained by Gram, Koritschoner, Hoffmann" etc.

"Diuretin brought about a very considerable increase in the excretion of urine, the volume, in isolated cases, amounting 8—9 times as much as before the treatment. The favourable results were conspicuous in those cases where the dropsy was

to be regarded as due to obstruction of the general circulation i. e. where valvular insufficiency, etc., were present.”

**Dr. Th. K. Geissler** (Clinic of Prof. Tschudnowsky, St. Petersburg — Berl. klin. Wochenschrift 1891 No. 15—17) could confirm the powerful diuretic action of Diuretin in all cases. Not only the quantity of urine, but also that of the solid constituents, increased considerably. The author, therefore, characterised Diuretin as a true and powerful diuretic. As regards the explanation of the result, he differs from other authors, in tracing it, not alone to a stimulation of the renal epithelium, but also, in part, to a strengthening of the heart's action. He was able to demonstrate by means of the sphygmomanometer, in all cases, an increase of arterial pressure and a regulation of the pulse, and regards as a confirmation of this view, the fact that, the most marked diuretic effects were attained in valvular insufficiency, while, in myo-carditis, the success was less conspicuous. The strengthening of the hearts action, with a simultaneous stimulation of the secreting power of the renal epithelium, is a combination very favourable to diuresis.

**Dr. Kouindjy-Pomerantz** who carried out experiments with Diuretin in the Hôpital Cochin, Paris, under the direction of Prof. Dujardin-Beaumetz sums up her conclusions as under:

“Diuretin is an excellent diuretic, more powerful than caffeine, in doses of 45—75 grns *pro die*, given in quantities of 15 grains every two or three hours; it directly influences the renal epithelium.”

“No action on the heart could be observed. Diuretin brings about a rapid increase in the volume of urine and the diuresis lasts twice or three times as long as with caffeine. Habituation does not soon occur. Micturition is easy and does not cause burning in the urethra. The remedy has no action on the central nervous system. It is administered in milk or chocolate between meals. In cases of dropsy where diuresis was still possible the success was marked while it did not follow when the kidneys had undergone great changes.

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## Methods of Use.

Diuretin, which is readily soluble in warm water, is best given in the form of mixture, either simply in aqueous solution (5:100) or with the addition of correctives of which the best are Ol. menth. piper., Aq. menth. piper. or fœnicul. with some simple syrup.

Addition of acid or acid vegetable juices should be strictly avoided as otherwise the theobromine will be thrown out and fall to the bottom of the mixture as a thick white sediment.

Diuretin may also be administered in gelatine coated pills.

It is not desirable to prescribe Diuretin as powder, as, through the absorption of carbonic acid from the air, a part of the theobromine is soon displaced from the sodium combination and becomes insoluble.

The *daily dose* of Diuretin is 90 to 105 grains. The single dose about 15 grains.

The *price* of Diuretin has now been so far reduced that the remedy is more generally accessible.

## Formulæ:

R. Diuretin-Knoll . . 75—105 grains  
Aq. destill. . . . 4 fl. ounces.

M. D. S. To be given throughout the day in tablespoonfuls.

R. Diuretin-Knoll . . 75—105 grains  
Aq. destill. . . . 3 ounces  
Aq. Menth. pip. . . 3 ounces.

M. D. S. To be given throughout the day in tablespoonfuls.

## Clinical observations on the use of Diuretin at the St. Francis Hospital

by

A. Seibert, M. D.

(*Medical Record, New York, 1891, September*).

It would take too much time and space to mention all cases in which diuretin was given, and therefore I will describe but one case of each category.

*Acute Nephritis*.—Male, aged thirty, alcoholic history. Admitted January 10, 1891. On December 27th, patient had noticed shortness in breathing, swelling of feet, and diminution of urine. On admission, he presented hypostasis of left lower lobe of lung, marked œdema of face and lower extremities, scanty urine, fifty per cent. albumin (by volume), hyaline and granular casts. Ordination: Diuretin, 10.0 ( $\frac{1}{2}$  ounce), aq. destill., 180.0 (6 ounces), a tablespoonful every two hours.

Quantities of urine (for twenty-four hours) in ounces :

January 12th	} Diuretin.	= 38 ounces.	January 18th	= 87 ounces.
" 13th		= 42 "	" 20th	= 94 "
" 14th		= 48 "	" 21st	= 98 "
		58 "	" 23d	= 110 "
		76 "	" 25th	= 116 "
			" 26th	= 119 "

On February 6th all œdema had disappeared; albumin present in but small quantity; general condition much improved; lungs clear; appetite good. Discharged at request. During the test, the same moderate quantity of fluids was given. Pulse strong and normal since day after diuretin was all taken.

*Nephritis Chronica*.—Male, aged thirty; general œdema. Pulse 96.

Quantities of urine in ounces, from June 1st to 27th, diuretin (10 to 180) taken on June 2d, 3d and 4th: 24, 11, 12, 18, 14, 17, 20, 22, 29, 36, 71, 66, 84, 69, 73, 67, 90, 113, 116, 137, 115, 110, 67, 68, 55, 35, 63, 41, 64, 56, 67, 82, 72.

June 27th.—Albumin and œdema have disappeared; appetite good. Pulse normal, strong, and full since third day after diuretin was taken.

*Stenosis Aortæ, Insuff. Valv. Mitralis*.—Male, aged fifty-three; albumin; general œdema; bronchitis; pulse 110; hypostasis; dyspnœa; alcoholic history. Admitted June 15th.



Quantities of urine in ounces from June 16th to July 1st: 27, 22, 28, 34, 52, 67, 84, 98, 110, 126. June 27th, œdema has disappeared; pulse has become normal, strong and full, improving twenty-four hours after diuretin was taken; no albumin.

*General Remarks.*—In all cases, an even quantity of fluid was given to the patients. It is of importance to note, that the diuretic action of the drug increased from day to day, until two to three weeks after it had been taken, thus showing that the irritation or stimulation of the kidney epithelium continues for a long time—to my mind, one of the greatest virtues a remedy can have. In a number of cases of fatty heart, cirrhosis of liver, and far advanced cases of parenchymatous nephritis (where but little epithelium was left in the kidneys), no action appeared from this drug at all, even though the above dose was repeated four to six times within a few weeks; with other cases in private practice, I have in all given diuretin to twenty-five patients, and can sum up my notes in the following: Diuretin is a powerful diuretic in doses of ten to twelve grammes given in forty-eight hours, in cases of valvular heart lesions, acute and chronic nephritis. It is also an excellent heart stimulant, increasing blood-pressure, reducing abnormal frequency, and correcting irregularity of heart action. No bad effects were ever noticed even where ten grammes were given repeatedly without the desired effect. Naturally, wherever diuretic action appears, the heart's action improves, and where the one fails the other does also.

In accordance with other observers, no action whatever was noticed by me from this drug in cases of cirrhosis hepatis, fatty heart, aneurysma aortæ, and in far advanced cases of chronic nephritis, so that the latter fact may be of use for prognostic purposes. As Geisler also had prompt action in a case of acute scarlatinal nephritis in an adult, this new remedy will undoubtedly be used with much benefit in acute nephritis following infectious diseases of children (scarlatina, varicella, pneumonia, morbilli, etc.), because it may safely be employed with benefit to kidneys and heart.

## Note upon a possible service to be expected from Diuretin in Genito-Urinary Surgery

by

Edward L. Keyes, M. D.,  
New York.

(*Medical News, Philadelphia, 1891, October*).

To prevent urinary fever various things have been done: all kinds of preparation of the patient, and the use of drugs—notably aconite, pilocarpine, quinine, etc.—ordered. I never thought well of aconite; I did once confide in pilocarpine, but gave it up. I have long since ceased to use quinine; I now never administer it before an operation, believing it to be absolutely devoid of value. Local urethral antiseptics I believe to be much overrated.

But this article is not to detract from the value of the means that we have to render urethral and bladder surgery more safe. It is to suggest another, in the hope that there may be value in it.

In June last I went to a city near New York to take a large stone from the bladder of an old gentleman, and at the same time to remove an outstanding third lobe. His case was desperate. He had suffered long, and for four years he had been an invalid, spending most of the last year in bed, taking opium suppositories, and passing his catheter hourly sometimes, and again at longer intervals. He could not urinate at all without the catheter. I cut this patient above the pubes, and took out a stone as large as an egg and a prostatic third lobe as large as the last joint of the thumb. The bladder was thin-walled, corrugated, trabeculated, and sacculated. I put my finger into holes on each side which seemed like ureteral orifices, but did not stop to investigate closely. They could not have been orifices of the ureters, because these are closed even when the ducts are enormously dilated. His urine had been like gruel, full of albumin and all sorts of detritus. There was no question of there being dilated ureters, pyelitis, and more or less interstitial nephritis on both sides. The operation was done simply because it had to be done in compassion for the old man's sufferings. The outlook was desperate.

I thought, then, of trying diuretin, and telephoned for it before the patient recovered from his anesthetic, ordering 10 grains to be given at once, and frequently repeated. This patient got well.

Since that time I have used diuretin in every case of urethral or bladder operation that has fallen under my hands. I give 60

grains of salol per day for forty-eight hours before operating, and commence diuretin on the day of the operation, given it also in doses of 10 grains every four hours for forty-eight hours. I, of course, irrigate the bladder and urethra; I did this before, but my results have been better since using the diuretin. I have used it in every major operation that I have performed, and my assistant, Dr. Fuller, has used it twice, and in no instance has there been any urinary fever proper—that is, there never has been a chill or a suppression. The cases cover all ages from eighteen to eighty, with desperate complications, such as pyelitis, urine loaded with albumin and casts, diabetes, etc. Patients have had shock, fever sometimes, and various complications, but never chill or suppression. The number operated on is 13; not large, it is true, but it was in the summer season, and all were private patients. The time is too short for generalization, but when it is remembered that the cases were: Supra-pubic prostatectomy, 6; supra-pubic lithotomy (diabetes), 1; perineal section, 3; perineal section without guide, 2; litholapaxy, 1; mostly in old men with damaged kidneys, all of whom recovered without chill or any tendency to suppression, it is fair to imagine that the means used had something to do with it, and the diuretin is the only new drug. In three of the cases there was profound shock after the chloroform (which I now always use), but the kidneys acted all along.

Diuretin appears to be a free diuretic, seemingly pretty constant in its action. It does not irritate the stomach, bowels, or nerves, and does not depress a weak heart. The dose 15 grains often repeated, to 90 or even 120 grains a day, given in freshly prepared aqueous solution, as the powder deteriorates on exposure. If it will prevent, or even moderate urinary fever, it is a valuable drug.

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## CAUTION!

All the observations in this pamphlet have reference to the use of the preparation of Knoll & Co.; as there are imitations in the market, physicians should see that the genuine is supplied. It is put up only in original vials of one ounce, and is plainly labeled DIURETIN-KNOLL.



